The analysis of sensitivity, specificity, positive predictive value and negative predictive value of cold provocation thermography in the objective diagnosis of the hand–arm vibration syndrome

P. A. Coughlin, I. C. Chetter, P. J. Kent and R. C. Kester
Department of Vascular and Endovascular Surgery, St. James’s and Seacroft University Hospitals, Leeds LS9 7TF, UK

The diagnosis of digital artery vasospasm in the hand–arm vibration syndrome (HAVS) is clinically based, and the need for an accurate objective test to support the diagnosis has been highlighted. This study aims to analyse the potential of cold provocation thermography (CPT) to fulfil this role. CPT was performed on two groups of subjects: 10 controls and 21 patients with Raynaud’s phenomenon (RP) secondary to HAVS. After taking a pre-cooling image, patients donned latex gloves and immersed their hands in water at a temperature of 5°C for 1 min. The patients removed their hands from the water and discarded the gloves, and further images were taken every 30 s for 10 min. On each image, the temperatures of the tip and base were analysed for each digit. The sensitivity, specificity, positive and negative predictive values for fingertip temperatures only, fingertip and fingerbase temperatures combined, and fingertip temperature, fingerbase temperature and temperature gradient combined were determined. Patients with RP secondary to HAVS demonstrated significantly lower finger tip and base temperatures and lower digital temperature gradients at all time intervals when compared with controls (P < 0.01, Student’s t-test). CPT has good sensitivity, specificity, positive predictive value and negative predictive value; it strongly supports the clinical diagnosis of digital vasospasm.

Key words: Cold provocation thermography; hand–arm vibration syndrome.

Introduction
Raynaud’s phenomenon (RP), characterized by episodic colour changes of the fingers and/or toes on exposure to cold or emotional stress, may occur as an isolated condition (primary RP) or may be associated with an underlying disease (secondary RP). Occupational vibration exposure is a recognized cause of secondary RP as part of the hand–arm vibration syndrome (HAVS). HAVS is a complex condition characterized by vascular, neurological and musculoskeletal disorders, primarily of the upper limb [1]. Recent estimations suggest that within the UK, 1.2 million workers are exposed to vibration at levels at which the Health & Safety Executive (HSE) recommends that employers should be taking action, and 242,000 cases of extensive cold-induced finger...
blanching are likely to be attributable to hand–arm vibration [2]. Since 1985, when HAVS became a prescribed disease in the UK under the National Insurance (Industrial Injuries) Act, the number of claimants seeking compensation and disability benefit has increased steadily. As a result, HAVS is presently the commonest prescribed disease in the UK [3,4]. Given the scale of the problem and the medico-legal implications of this clinical diagnosis, it has been highlighted that physicians should attempt to supply objective evidence to support the diagnosis [5]. Observation of colour changes in the fingers following immersion in cold water is notoriously unreliable. Previous studies of patients with RP have measured finger temperatures using thermocouples following cold provocation, but the sensitivity of the technique is disputed [6–9]. Griffin et al. [10] say that ‘the repeatability of the tests was found to be acceptable for routine diagnosis and screening of vibration induced white finger’. However, they go on to say: ‘Amongst manual workers and subjects with VWF, test results were more variable than for office workers . . .’.

Thermal imaging is another method used to measure finger temperature, and it offers the flexibility of being able to measure temperatures of any part of the hand or fingers as well as reducing the amount of manipulation of the patient’s hands that is needed to fix on the thermocouples. This study aims to determine the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of finger temperatures measured using infrared thermal imaging following standardized cooling.

Patients and methods

Two groups of subjects were studied. Written informed consent was obtained from all participants.

Group A comprised 10 normal healthy volunteers—five men and five women—median age 35 years (range 24–78 years), who had no past history of vibration exposure or symptoms suggestive of RP. No subjects were taking any medication known to affect the vascular tree and they were all asked to refrain from smoking for the 24 h period prior to the test.

Group B comprised 21 consecutive patients—20 men and one woman—median age 45 years (range 29–81 years), with RP secondary to HAVS. All patients underwent a thorough historical and physical examination performed by a single physician, and immunological, biochemical and haematological tests were performed to exclude any known causes of secondary RP. All patients were graded as Stockholm Workshop scale 3 [11].

Cold provocation thermography (CPT) was performed on all subjects. The subjects’ temperature was equilibrated by placing them in a room with an ambient temperature of 25°C for 45 min, following which a pre-cooling thermal image of the palmar aspects of the subjects’ hands was taken using a thermal imaging camera (Insight Vision Systems Ltd, Malvern, UK). Subjects then donned a pair of thin, closely fitting, latex gloves and placed their hands into water at a temperature of 5°C. After 1 min of cold immersion, subjects removed their hands from the water and discarded the gloves, and further thermal images were then taken every 30 s for the following 10 min of passive rewarming. On each of the 21 images obtained from each subject, temperature readings were taken from the tips and bases of all digits. The temperature gradient for each digit on each image was calculated by subtracting the temperature of the base from that of the tip.

Statistical analysis

The results were analysed on a personal computer using a commercial statistical program (Astute, Leeds University and Microsoft Excel, UK).

Results

Prior to cooling and at each time point during rewarming, digit tip temperatures of HAVS patients were significantly lower than those of controls ($P < 0.01$, $t$-test; Figure 1). Digit tip temperature of controls recovered to pre-cooling values by 4 min ($P > 0.01$, paired $t$-test), whilst the digit tip temperatures of HAVS patients remained significantly lower than pre-cooling values until the end of the test ($P < 0.01$, paired $t$-test).

Prior to cooling and at each time point during rewarming, digit base temperatures of HAVS patients were significantly lower than those of controls ($P < 0.01$, $t$-test; Figure 2). Digit base temperatures of controls recovered to pre-cooling values by 6.5 min ($P > 0.01$, paired $t$-test), whilst the digit base temperatures of HAVS patients remained significantly lower than pre-cooling values until the end of the test ($P < 0.01$, paired $t$-test).

Prior to cooling, there was no significant temperature gradient between digit tips and digit bases in control patients ($P > 0.01$, $t$-test). However, in the HAVS patients, the digit tips were significantly cooler than digit bases, resulting in a negative temperature gradient along the digit ($P < 0.01$, $t$-test; Figure 3).

During rewarming in the control patients, at 3.5 min and at each time point following this, finger tip temperatures were significantly higher than base temperatures ($P < 0.01$, $t$-test), resulting in a positive digit temperature gradient, indicating that the digit tips rewarmed more quickly than the digit bases. During rewarming in the HAVS subjects, digit tip temperatures were significantly lower than digit base temperatures until 6.5 min ($P < 0.01$, $t$-test), resulting in a negative digit temperature
gradient, indicating that the digit bases rewarmed more quickly than the digit tips.

Using a single summary measure of time taken to return to pre-cooling temperature, it can be seen that there is a significant difference between the HAVS group and the control group for both fingertip and fingerbase measurements, as well as the time taken for the temperature gradient to return to a positive value.

**Figure 1.** Fingertip temperatures (means and SD).

**Figure 2.** Fingerbase temperatures (means and SD).

**Figure 3.** Finger temperature gradients (means and SD).
There are a number of patients whose fingertip and fingerbase temperatures had not returned to pre-cooling levels by the end of the rewarming period. These patients were given rewarming times of 10 min. Therefore, the median values obtained in the patient group are likely to be an underestimation.

Table 2 shows the sensitivity, specificity, PPV and NPV of the fingertip temperatures following cold provocation, both pre-cooling and throughout the rewarming period. Pre-cooling, CPT had both good specificity and PPV, although low sensitivity. Immediately following pre-cooling, the sensitivity of the test fell to 24% but rose rapidly to 95% at 3 min. The sensitivity remained high throughout the remainder of the rewarming period. The test was at its most specific in the first 3 min following cooling, maintaining a specificity of 100%. This value fell slightly during the rewarming period, resulting in a specificity of 75% at 10 min. The PPV remained ≥90% both pre-cooling and throughout the rewarming period. The NPV was 50% pre-cooling, and following cooling, was maintained at 30% up to 3 min. After this time, the NPV rose to 88%, further rising to 100% at 7 min. The NPV then fell at 9 min to 78%, falling further to 67% at 10 min. Determination of HAVS appears to be most accurate at 8 min, with a sensitivity of 100%, a specificity of 88%, a PPV of 95% and an NPV of 100%.

Following this, we determined the accuracy of CPT using the fingertip temperatures, the fingerbase temperatures and the finger gradients (Table 4) as a marker of disease (i.e. patients with a disease-negative mean fingertip temperature and a subsequent disease-negative mean fingerbase temperature were then considered to have the disease if the subsequent mean fingerbase temperature was >2 SD away from the mean control temperature). There was no change in any of the values compared with the fingertip temperatures alone, both pre-cooling and up to 8 min after commencement of rewarming. After 9 and 10 min, however, the sensitivities and NPVs were both increased: from 90 and 78% to 100 at 9 min, and from 86 and 67% to 90 and 75% at 10 min. Again, determination of HAVS appears to be most accurate at 8 min, with a sensitivity of 100%, a specificity of 88%, a PPV of 95% and an NPV of 100%.

It is interesting to note that the test was most accurate in determining the presence or absence of disease at 8 min following the onset of rewarming. In each of the three

### Table 1. Table comparing the time taken for temperatures to return to pre-cooling levels and for temperature gradients to return to positive levels [median values (interquartile range)]

<table>
<thead>
<tr>
<th></th>
<th>HAVS</th>
<th>Controls</th>
<th>P value (Mann–Whitney U-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fingertip temperature: time taken to return to pre-cooling temperature following cooling (min)</td>
<td>10 (8–10)</td>
<td>3 (2.88–5.38)</td>
<td>0.001</td>
</tr>
<tr>
<td>Fingerbase temperature: time taken to return to pre-cooling temperature following cooling (min)</td>
<td>10 (10–10)</td>
<td>6.25 (4.88–8.88)</td>
<td>0.006</td>
</tr>
<tr>
<td>Temperature gradient: time taken to return to positive value following cooling (min)</td>
<td>9.5 (6.5–10)</td>
<td>1.5 (0.75–2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Table 2. Accuracy of CPT (fingertip temperatures)

<table>
<thead>
<tr>
<th>Time</th>
<th>Pre</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>67</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>95</td>
<td>95</td>
<td>90</td>
<td>95</td>
<td>100</td>
<td>100</td>
<td>90</td>
<td>86</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>88</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>75</td>
<td>88</td>
<td>88</td>
<td>75</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>93</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>88</td>
<td>88</td>
<td>95</td>
<td>95</td>
<td>95</td>
<td>95</td>
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</tr>
<tr>
<td>NPV (%)</td>
<td>50</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>88</td>
<td>88</td>
<td>78</td>
<td>88</td>
<td>100</td>
<td>100</td>
<td>78</td>
<td>67</td>
</tr>
</tbody>
</table>

Lower normal limits (mean – 2 SD) taken from control group.
tables (Tables 2–4) the values obtained for each calculation are at their highest at this time point. Again, determination of HAVS appears to be most accurate towards the end of the test, at 7, 8 and 9 min, with a value of 100% for all values.

**Discussion**

HAVS is becoming an increasing part of the workload of vascular surgeons, occupational physicians and medical works officers. At present, the diagnosis is subjective, relying on the patient’s history together with a history of occupational exposure to vibration and the exclusion of other known causes of RP [1]. There are as yet no gold standard objective tests for the diagnosis of HAVS. Disease severity is graded using the Stockholm Workshop scale, which relies mainly on subjective findings [11]. Therefore, there is the need for a suitable objective investigation to confirm the diagnosis of vasospasm. However, the diagnostic method must have good sensitivity, specificity and reproducibility [5]. Many objective tests have been used to detect circulatory impairment in HAVS [1], but as yet there is a lack of consensus regarding their accuracy. In the laboratory setting, plethysmography, Doppler ultrasound and radioactive isotope clearance methods have been used to measure digital blood pressures and flow. Infrared thermography has been used to study skin temperature distribution.

Finger skin temperature is considered a useful physiological parameter to monitor the digital vasculature following cold provocation [8]. Cold is thought to precipitate vasospasm of the digital vessels, and the rewarming pattern is believed to correlate with the degree of vasospasm.

Using thermocouples, Welsh [6] looked at the rewarming times following cold provocation in people with primary RP and HAVS, and compared them with a control group. He found that the people with RP and HAVS had significantly prolonged rewarming times compared with the control. Pelmear et al. [13] found sufferers to have significantly reduced finger temperatures following cold provocation compared with a control group. They also found that finger temperature following cold provocation varied with disease severity. Kurumantani et al. [7] found finger skin temperature to be both sensitive and specific in the diagnosis of HAVS, although Bovenzi found it to have a sensitivity of only 60% and suggested that finger systolic pressure measurements should be used to confirm the diagnosis. He believed that the combination of environmental and individual factors were contributory to the lack of sensitivity [8].

In this study, all environmental conditions were maintained at a constant level. Ambient temperature was maintained at 25°C, and all patients were allowed to equilibrate with this temperature for 45 min. A standard provocation using water of temperature 5°C was used, and the hands covered in latex gloves during the 1 min of cooling to prevent the cold water coming into contact with the flesh. The subsequent effect of evaporation would have a cooling effect on the hands. Many studies have used a longer cooling time and various water tempera-
tures. A short cooling period was used in our study to reduce the chance of paradoxical vasodilatation of the digital arteries (the Hunting reaction) [14]. No patients in this study complained of any undue discomfort owing to the temperature of the water used. During the rewarming period, patients were placed in an environmental chamber, which regulated air temperature, relative air velocity and humidity. We have demonstrated in our study that fingertips (which have a greater vascularity in the pulp spaces than the finger bases) rewarm more quickly than their fingerbases in normal subjects, but conversely patients with HAVS have a reversed pattern of rewarming whereby the fingerbases rewarm at a faster rate than the corresponding fingertips. Therefore, although initial one-off pre-cooling temperature measurements offer us a reasonable diagnostic clue regarding the presence or absence of disease, the rewarming is needed to confirm the reversed rewarming pattern that is characteristic of vasospastic disease.

The results of our study show that finger temperature following cold provocation and the time taken for finger temperatures to return to pre-cooling levels were able to distinguish between the patients with HAVS and the control group. The specificity and PPVs were high throughout the test. The sensitivity of CPT was initially low following cooling, but after 3 min of rewarming the values were high, reaching a maximum of 95%. The use of a combination of fingertip temperature followed by the subsequent fingerbase temperature (if a positive diagnosis could not be made using solely the fingertip temperature) improved the accuracy of diagnosis towards the end of the rewarming period, at 9 and 10 min. The use of a combination of fingertip temperature and fingerbase temperature followed by the subsequent finger temperature gradient (if a positive diagnosis could not be made using solely the fingertip temperature and fingerbase temperature) improved the accuracy of diagnosis throughout the whole of the test. We also showed that the accuracy of the test was at its greatest towards the latter stages of the rewarming period.

The diagnosis of HAVS can be difficult to make. It is based upon the presence of symptoms, with an occupational history of vibration exposure and the exclusion of other known causes of secondary RP. At present there is no single gold standard test. Because of the potential difficulties in diagnosing the condition and the lack of understanding of the condition by some physicians, the exact prevalence of HAVS is difficult to determine. Recent estimations suggest that ~242 000 cases of extensive cold-induced finger blanching are likely to be attributable to hand–arm vibration [2]. Our establishment is a tertiary referral centre and the proportion of patients that we see who actually have HAVS is high. As the exact prevalence is unknown, the PPV in this study may not be representative if applied universally.

However, our initial study here shows that if environmental conditions are constant, CPT is an accurate objective diagnostic investigation for HAVS. Given the current lack of, but increasing need for an accurate objective investigation for HAVS, our results lend weight to the use of CPT as a standard objective investigation in the assessment of patients with HAVS.

Acknowledgements

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References